

**Remarks**

Favorable reconsideration in view of the herewith presented amendment and remarks is respectfully requested.

Claims 4, 5, 8 and 11 are pending in this application. Claims 1-3, 6, 7, 9 and 10 are cancelled.

Claim 4 is objected to because of informalities. Claim 4 has been amended using the Examiner's suggestions. Withdrawal of this formal objection is requested.

Claims 5 and 10-11 are rejected under 35 U.S.C. 112 as failing to comply with the written description requirement.

Claim 5 has been amended in the manner suggested by the Examiner. It is believed this rejection has been overcome and withdrawal of the rejection is requested.

Claim 9 is rejected under 35 U.S.C. 112 as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

This rejection is believed to be moot.

Claim 5 is rejected under 35 U.S.C. 103(a) as being unpatentable over Desmyter et al. taken with YANO 1.

Claim 4 is rejected under 35 U.S.C. 103(a) as being unpatentable over Desmyter et al. taken with YANO 1 et al. as applied to claim 5, and further in view of Bever et al.

Claims 5 and 10-11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Desmyter et al. taken with YANO 1 as applied to claim 5, and further in view of Yano 2.

Claims 4 and 7-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Desmyter et al. taken with YANO 1, and Bever et al. as applied to claim 4, and further in view of Yano 2.

Claims 4 and 6 are rejected under 35 U.S.C. 103(a) as being unpatentable over either Desmyter et al. taken with YANO 1 in further view of Bever et al. as applied to claim 4, and further in view of Liaw.

Claims 5 and 9 are rejected under 35 U.S.C. 103(a) as being unpatentable over either Desmyter et al. taken with and YANO 1 as applied to claim 5, and further in view of Liaw.

Applicants respectfully traverse these rejections.

The Examiner alleges that the prior art (e.g., Desmyter) teaches one of ordinary skill in the art that delivering 3 mg of Poly IC to a mammal was a well known concentration for delivering Poly IC to a mammal. Further, the Examiner asserts that the specification does not teach any unexpected result from using 3 mg of Poly IC, which falls within the range of 1  $\mu$ g to 50 mg of Poly IC in the method.

Applicants disagree with the Examiner. Desmyter does not disclose delivering 3 mg of Poly IC to a mammal. The dosage of Poly IC for delivering to a mammal taught by Desmyter is 3mg/kg which does not fall within the range of 1  $\mu$ g to 50 mg/human of Poly IC in the present claims. The dosage of Poly IC in the present claims is much lower than that in Desmyter.

The Examiner is also of an opinion that in view of using the method taught by Desmyter and the routes taught by YANO 1, one of ordinary skill in the art would have expected that by intravenously or transmucosally administering Poly IC to a human would induce interferon chiefly in the liver of a human with a reasonable expectation of success.

While Desmyter teaches that the administration of Poly IC to a mammal results in direct action of interferon in the liver as the Examiner admits in line 5, page 5 of the office action, Desmyter does not teach at all that the administration of Poly IC to a mammal can induce the expression or production of interferon chiefly in the liver.

The complex of the present invention is accumulated in the liver by 80% and can induce interferon especially in the liver. Since the hepatitis virus increases only in the liver, it is very reasonable to induce interferon chiefly in the liver. If interferon is induced chiefly in the liver, toxicity in organs other than liver could be much less than expected.

In addition, Desmyter and Bever use a complex of poly-L-lysine and carboxymethylcellulose with Poly IC (Poly ICLC). Poly ICLC is not a complex of a cationic liposome with Poly IC in connection with the present invention. Namely, poly-L-lysine and carboxymethylcellulose do not compose a cationic liposome.

In view of these points, the administration of complex of the present invention is entirely different from that of interferon itself, Poly IC alone, or Poly ICLC in pharmacological action or effect.

Further, the Examiner states that one of ordinary skill in the art would have been motivated to use Poly IC which has a mean length within the range of 100 to 500 bp as taught by YANO 1 for inducing interferon chiefly in the liver of a human because this range displays reduced toxicity of the double stranded RNA in vivo.

YANO 1 teaches that the fact that control of molecular size of nucleic acid polymer within a specified range is primarily the important factor for the remarkable reduction of toxicity of Poly IC and the preferred molecular size for using Poly IC is from 100 to 600 base numbers as

the Examiner admits in the 6<sup>th</sup> line to 3<sup>rd</sup> line from the bottom of page 5 in the office action. However, YANO 1 does not teach if the chain-shortened Poly IC can induce interferon chiefly in the liver in an amount sufficient to treat hepatitis in a human. On the other hand, Desmyter and Bever teach that when Poly ICLC was administered to chronic hepatitis B models of chimpanzees and patients with multiple sclerosis (MS), hepatitis B virus (HBV)-related antigens in chimpanzees were suppressed and interferon of substantial level was produced in MS patients. However, neither Desmyter nor Bever teaches about the toxicity of the Poly ICLC.

The present invention teaches that 1  $\mu$ g-50 mg of Poly IC which has a mean length within the range of 100-500 bp in the complex has markedly less toxicity, and at the same time it can induce a substantive amount of interferon chiefly in the liver enough to treat hepatitis. It would not have been obvious for a person of ordinary skill to get both the induction of interferon chiefly in the liver in an amount sufficient for the treatment of hepatitis and at the same time markedly lower toxicity by administering the complex of the present invention. The present invention is urged patentable over the prior art.

None of the other prior art relied upon by the Examiner remedies the deficiencies noted above in the primary citations.

Reconsideration and withdrawal of all the Examiner's §112 and §103 rejections is respectfully requested.

It is believed that all of the present claims are in condition for allowance. The Examiner is requested to reconsider and withdraw all of the rejections made in the Official Action. Early and favorable action by the Examiner is earnestly solicited.

## AUTHORIZATION

If the Examiner believes that issues may be resolved by telephone interview, the Examiner is respectfully urged to telephone the undersigned at (212) 801-2146. The undersigned may also be contacted by e-mail at [ecr@gtlaw.com](mailto:ecr@gtlaw.com).

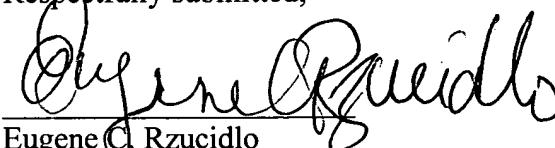
No additional fee is believed to be necessary. The Commissioner is hereby authorized to charge any additional fees which may be required for this amendment, or credit any overpayment to Deposit Account No. 50-1561.

In the event that an extension of time is required, or which may be required in addition to that requested in a petition for an extension of time, the Commissioner is requested to grant a petition for that extension of time which is required to make this response timely and is hereby authorized to charge any fee for such an extension of time or credit any overpayment for an extension of time to Deposit Account No. 50-1561.

Respectfully submitted,

Dated: May 26, 2005

By:

  
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